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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

DUE DATE:	
FORMALITIES:	C.N. R.P.
PAT. OFF:	A.K.
ON DB	
CASE NO.:	PU0378-PCT

Applicant's or agent's file reference PU0378-PCT ✓	FOR FURTHER ACTION See Form PCT/IPEA/416	
International application No. PCT/SE2004/001583 ✓	International filing date (day/month/year) 01-11-2004 ✓	Priority date (day/month/year) 31-10-2003
International Patent Classification (IPC) or national classification and IPC See Supplemental Box		
Applicant Amersham Biosciences AB et al		

- This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
- This REPORT consists of a total of 7 sheets, including this cover sheet.
- This report is also accompanied by ANNEXES, comprising:
 - ☐ (sent to the applicant and to the International Bureau) a total of _____ sheets, as follows:
 - ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
 - ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
 - ☐ (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) _____, containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

- This report contains indications relating to the following items:

- | | | |
|-------------------------------------|--------------|---|
| <input checked="" type="checkbox"/> | Box No. I | Basis of the report |
| <input type="checkbox"/> | Box No. II | Priority |
| <input type="checkbox"/> | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| <input type="checkbox"/> | Box No. IV | Lack of unity of invention |
| <input checked="" type="checkbox"/> | Box No. V | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input type="checkbox"/> | Box No. VI | Certain documents cited |
| <input type="checkbox"/> | Box No. VII | Certain defects in the international application |
| <input checked="" type="checkbox"/> | Box No. VIII | Certain observations on the international application |

Date of submission of the demand 10-05-2005	Date of completion of this report 27-12-2005
Name and mailing address of the IPEA/SE Patent- och registreringsverket Box 5055 S-102 42 STOCKHOLM Facsimile No. +46 8 667 72 88	Authorized officer Jens Waltin / MRO Telephone No. +46 8 782 25 00

Form PCT/IPEA/409 (cover sheet) (April 2005)

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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/SE2004/001583

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of: **Cover sheet**

INTERNATIONAL PATENT CLASSIFICATION (IPC) :

B01D 15/26 (2006.01)

B01D 15/32 (2006.01)

B01D 15/36 (2006.01)

B01D 15/38 (2006.01)

B01J 20/28 (2006.01)

B01J 20/30 (2006.01)

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

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Box No. I Basis of the report

1. With regard to the language, this report is based on:



the international application in the language in which it was filed



a translation of the international application into _____,
which is the language of a translation furnished for the purposes of:



international search (Rules 12.3(a) and 23.1(b))



publication of the international application (Rule 12.4(a))



international preliminary examination (Rules 55.2(a) and/or 55.3(a))

2. With regard to the elements of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:



the international application as originally filed/furnished



the description:

pages _____ as originally filed/furnished

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____



the claims:

pages _____ as originally filed/furnished

pages* _____ as amended (together with any statement) under Article 19

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____



the drawings:

pages _____ as originally filed/furnished

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____



a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:



the description, pages _____



the claims, Nos. _____



the drawings, sheets/figs _____



the sequence listing (*specify*): _____



any table(s) related to the sequence listing (*specify*): _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).



the description, pages _____



the claims, Nos. _____



the drawings, sheets/figs _____



the sequence listing (*specify*): _____



any table(s) related to the sequence listing (*specify*): _____

* If item 4 applies, some or all of those sheets may be marked "superseded."

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

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Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	<u>4.8.11-15.20-31.33.37.40-44.52</u>	YES
	Claims	<u>See Supplemental Box</u>	NO
Inventive step (IS)	Claims	<u>4.8.15.20-31.44</u>	YES
	Claims	<u>1-3.5-7.9-14.16-19.32-43.45-53</u>	NO
Industrial applicability (IA)	Claims	<u>1-53</u>	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

The invention relates to a chromatography matrix, wherein the ligands provide a chemical gradient in the support. This leads to improved mass transport properties during adsorption and desorption.

The most relevant documents cited in the International Search Report are:

D1: US6426315 B1
D2: US5561097 A
D3: US6528322 B1
D4: US5977345 A

D1 relates to a process for preparing multifunctional porous separation matrices by introducing different functionalities in different layers of the matrix (col. 2, lines 1-45; col. 6, lines 17-26). The process includes contacting a separation matrix that comprises reactive groups with a reagent (e.g. activating agent), the amount of which is not sufficient for reaction with all groups present in the matrix. Desired functionality can be introduced in a subsequent step. The substitution degree of one ligand in one layer is often different from the substitution degree of the same ligand in another layer. A ligand in the surface layer can be zero and at the same time present in another layer. Also, the reverse can be true. Suitable matrices are in the form of particles (col. 3, line 47 - col. 4, line 38). Charged ligands can be used (col. 4, line 57 - col. 5, line 25).

The invention according to claims 1-3, 5-7, 9, 10, 16-19, 32, 34-36, 38, 39, 45-51 and 53 lacks novelty in view of D1.

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Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of: **BOX V**

NOVELTY, NO: 1-3, 5-7, 9, 10, 16-19, 32, 34-36, 38, 39, 45-51, 53

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of: BOX V

The remaining claims 11-14, 33, 40-43 and 52 are considered to involve particular detail executions obvious to a person skilled in the art. Therefore, the invention according to these claims is not considered to involve an inventive step.

Claims 33 and 37 relates to two methods of coupling ligands to the separation matrix. These methods are not disclosed in D1. However, they are both known through D2. The first method is disclosed in the background art of D2 (col. 1, lines 22-26) and the second method is disclosed in the detailed description (col. 3, lines 58-66 and col. 5, line 24-35). The use of these methods in the invention according to claims 33 and 37 has not been shown to give rise to any unexpected effects. It is therefore considered to be obvious to a person skilled in the art to use the methods described in D2 in order to produce a matrix with a ligand density gradient as disclosed in D1. Consequently, the invention according to claims 33 and 37 lacks an inventive step with respect to D1 in combination with D2.

The invention also lacks novelty in view of D3. D3 discloses an analytical method for determination of two analytes in a sample by thin layer chromatography. The separation zone may have different ligand densities or a gradient of ligand densities along the separation direction.

The invention according to claims 1, 3, 10, 47, 49, 50 and 53 lacks novelty in view of D3.

See also D4, which discloses chromatographic affinity matrices with higher concentration of ligand or ionic moiety in the intra-particle volume than the outer matrix surface (abstract and claims).

The invention according to claims 1-3, 11-14, 16-19 and 47-53 lacks novelty in view of D4.

The invention according to claims 4, 8, 15, 20-31, 44 is however novel and considered to involve an inventive step.

The invention is also considered to be industrially applicable.

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

The term "solvent controlled diffusion" used in claim 20 is vague and unclear and leave the reader in doubt as to the meaning of the technical feature to which it refers, thereby rendering the definition of the subject-matter of said claim unclear (Article 6 PCT).

Claim 40 does not meet the requirements of Article 6 PCT in that the matter for which protection is sought is not clearly defined. The claim attempts to define the invention in terms of the result to be achieved, which merely amounts to a statement of the underlying problem. The technical features necessary for achieving this result should be added to the claim.

Claim 37 relates to independent claim 32 and the steps (a) - (c). These steps cannot be replaced by a single step as defined in claim 37 as it would conflict with the independent claim 32.

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